

EXHIBIT F2

February 6, 2019

To whom it may concern at Health Canada

I am a professor of epidemiology with particular interest and experience with research on risk factors for cancer. I attach a recent abbreviated CV to provide you with some idea of my training and experience. I have learned that Health Canada is proposing to implement some measures to encourage the restriction of use of cosmetic talc in Canada. I have also learned that Health Canada is inviting comments.

I have been involved in evaluating carcinogenicity of talc in two distinct contexts. In 2006 I was invited by the International Agency for Research on Cancer (IARC) in an expert working group to evaluate carcinogenicity of talc. I was asked to chair the international multidisciplinary working group. The IARC evaluations are considered the most authoritative evaluations of carcinogenicity in the world. After reviewing all evidence available at the time, our panel concluded that talc was possibly carcinogenic for the ovary of women who applied talcum powder products regularly to the perineal area. (IARC, 2010) Following that panel decision, some members, including myself, conducted a meta-analysis of epidemiologic data and published a paper. (Langseth, 2008)

In 2015 I was contacted by a lawyer who was working for plaintiffs who had ovarian cancer and who were suing the makers of talcum products and claiming that those products had caused their disease. I had not reviewed the evidence since the IARC panel of 2006. I agreed to review the evidence again and I did so in 2016 and conducted a new meta-analysis. I concluded that it was "more likely than not" that there was a causal association between body powdering with talcum powder and risk of ovarian cancer. This conclusion was based on evidence that had accumulated up to 2016. It included the following components:

- The number of epidemiologic studies had considerably increased between 2006 and 2016.
- Among approximately 30 epidemiologic studies that provided evidence on the talc-ovarian cancer association, all but one or two manifested relative risk estimates above 1.0. If there truly were no association we would expect half of the results to be above 1.0 and half below 1.0.
- Depending on some judgements calls on which studies and which results to include in the meta-analysis, the meta-RR was close to 1.28 with 95% confidence limits ranging from 1.19 to 1.38. The p-value for this RR was vanishingly small. This demonstrated that chance (random variability) could not be invoked as a possible explanation for the consistently observed excess risk.
- Whereas there was no evidence of dose response between amount of powdering and risk of ovarian cancer in 2006, in 2013 there was a publication (Terry, 2013) that pooled data from 8 different centers representing 10 different studies. This pooled dataset was the first one that afforded sufficient numbers of study subjects to evaluate the risk of ovarian cancer by different levels of cumulative exposure. This analysis showed increasing relative risk estimates across the five categories (non-users and four quartiles of cumulative exposures). The RR estimates were 1.00, 1.18, 1.22, 1.22, and 1.37. Each of the estimates in the four quartiles was statistically significant. The clear monotonic increase in RR among the five groups represents the main supporting evidence of dose-response that was absent in 2006.

- Before concluding that these numerically impressive results were due to a causal relationship, I carried out an exercise to consider all plausible sources of bias and confounding, including notably recall bias, non-differential measurement error, insufficient follow-up time, and others. I concluded that it was most unlikely that the observed associations are due to bias or confounding.
- The epidemiologic evidence is therefore reasonably strong and consistent in arguing for a causal association.
- No biological mechanism has been proven, but that is normal. Most known carcinogens (including tobacco smoke) had convincing epidemiologic evidence of causality long before there was any proof of the causal biological mechanism. There are however, plausible biological theories of how talcum powder use could lead to ovarian carcinogenesis, including evidence that particles deposited on the vagina can migrate to the ovaries, and that such particles can provoke chronic inflammation which can in turn provoke neoplastic change.

Further there is some recent evidence that talcum powder products may have been contaminated with asbestos fibres, which would add a degree of plausibility to this theory.

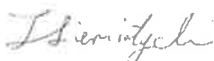
While I am aware of mechanistic theories that are plausible, I do not rely on the validity of those theories to conclude, on the basis of the epidemiologic evidence, that it is more likely than not that exposure to talcum powder products can cause ovarian cancer.

These are the views I expressed as an expert witness in a trial held in Los Angeles in 2017. And I have recently expressed these views in preparation for another U.S. trial.

While I was carrying out my meta-analyses, unbeknownst to me, two other teams were carrying out meta-analyses. These two have been published (Berge 2018, Penninkilampi 2018). There were a few minor differences in how the three meta-analyses were conducted, but they essentially found the same result. This reinforces my conclusion.

This lengthy exposition is a preamble to my conclusion that talcum powder products may be dangerous, and their use by women should be discouraged.

Yours truly,



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